W. Davis
661305

```
=> fil reg;del his y
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        38.32      79.74

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for details.


=> e nade/sqep 5
E1            1     NADDAFCRAMKRAGREVK/SQEP
E2            1     NADDCSYWLGELVWCVAGVE/SQEP
E3            0 --> NADE/SQEP
E4            1     NADFDGD/SQEP
E5            1     NADFKTPATLTVD/SQEP

=> s nade/sqsp
L1         1547 NADE/SQSP

=> e nade/cn 5
E1            1     NADC3 (RAT PLACENTA GENE NADC3 SODIUM-DEPENDENT
DICARBOXYLAT
                    E TRANSPORTER)/CN
E2            1     NADDS/CN
E3            0 --> NADE/CN
E4            1     NADEHP/CN
E5            1     NADEINE/CN

=> e apoptosis/cn 5
E1            1     APOPTIN/CN
E2            1     APOPTOLIDIN/CN
E3            0 --> APOPTOSIS/CN
E4            1     APOPTOSIS INHIBITOR PROTEIN (EPIPHYAS POSTVITTANA
NUCLEOPOLY
                    HEDROVIRUS GENE IAP-1)/CN
E5            1     APOPTOSIS INHIBITOR PROTEIN (EPIPHYAS POSTVITTANA
NUCLEOPOLY
                    HEDROVIRUS GENE IAP-2)/CN

=> s apoptosis?/cn
L2           54 APOPTOSIS?/CN
```


Prepared by M. Hale 308-4258

```
=> e p75ntr/cn 5
E1            1     P74RAF-1 PROTEIN KINASE/CN
E2            1     P75NGFR (RECEPTOR) (MUS MUSCULUS STRAIN A)/CN
E3            0 --> P75NTR/CN
E4            1     P76/CN
E5            1     P77/CN

=> e p75 neurotrophin receptor/cn 5
E1            1     P74RAF-1 KINASE/CN
E2            1     P74RAF-1 PROTEIN KINASE/CN
E3            0 --> P75 NEUROTROPHIN RECEPTOR/CN
E4            1     P75NGFR (RECEPTOR) (MUS MUSCULUS STRAIN A)/CN
E5            1     P76/CN

=> fil medl,caplus,biosis,embase,wpids,jicst
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              29.93     109.67

FILE 'MEDLINE' ENTERED AT 09:51:42 ON 10 AUG 2001

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FILE 'JICST-EPLUS' ENTERED AT 09:51:42 ON 10 AUG 2001
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=> s (l1 or nade or p75ntr or p75 neurotrophin receptor) and (l2 or
apoptosis? or capase or cell death or clonal delet?)
L3            97 FILE MEDLINE
L4           136 FILE CAPLUS
L5           128 FILE BIOSIS
L6            59 FILE EMBASE
'SQSP' IS NOT A VALID FIELD CODE
L7             8 FILE WPIDS
L8             3 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L9           431 (L1 OR NADE OR P75NTR OR P75 NEUROTROPHIN RECEPTOR) AND (L2 OR
                 APOPTOSIS? OR CAPASE OR CELL DEATH OR CLONAL DELET?)

=> s l9 and ("14-3-3" or nik hgk or p33 ing or eif4g or huntingtin bind?)
L10            1 FILE MEDLINE
```

L11 4 FILE CAPLUS
L12 0 FILE BIOSIS
L13 0 FILE EMBASE
L14 1 FILE WPIDS
L15 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L16 6 L9 AND ("14-3-3" OR NIK HGK OR P33 ING OR EIF4G OR HUNTINGTIN BIND?)

=> s l16 and (screen? or diagnos? or treat? ot therap? or prevent?)
L17 1 FILE MEDLINE
L18 3 FILE CAPLUS
L19 0 FILE BIOSIS
L20 0 FILE EMBASE
L21 1 FILE WPIDS
L22 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L23 5 L16 AND (SCREEN? OR DIAGNOS? OR TREAT? OT THERAP? OR PREVENT?)

=> dup rem l23
PROCESSING COMPLETED FOR L23
L24 3 DUP REM L23 (2 DUPLICATES REMOVED)

=> d cbib abs 1-3 hit;s l16 not l23

L24 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2001:208009 Document No. 134:231845 **NADE** binding proteins, and therapeutic agent **screening** method. Sato, Takaaki; Irie, Shinji (Riken Corp., Japan). Eur. Pat. Appl. EP 1085323 A2 20010321, 12 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-119976 20000914. PRIORITY: JP 1999-260947 19990914.
AB Agents for use in **screening** of medicaments for treatment, **prevention** and/or **diagnosis** of **apoptosis** -assocd. diseases are provided which comprise an **apoptosis** related protein binding to **NADE** (**p75NTR**-assocd. **cell death** executor) or a DNA encoding the protein.
TI **NADE** binding proteins, and therapeutic agent **screening** method
AB Agents for use in **screening** of medicaments for treatment, **prevention** and/or **diagnosis** of **apoptosis** -assocd. diseases are provided which comprise an **apoptosis** related protein binding to **NADE** (**p75NTR**-assocd. **cell death** executor) or a DNA encoding the protein.
ST drug **screening** **NADE** binding protein
IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(032345; **NADE** binding proteins, and therapeutic agent **screening** method)
IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**14-3-3**; **NADE** binding proteins,

and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AA207590; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AA277260; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AA413882; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AA499218; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AA717789; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AA755361; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AA794707; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AA967322; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(AU035250; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(C85116; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(DOCK; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Fam; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(GTP-binding, ran; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(KIAA0161; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(KIAA0181; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(KIAA0192; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(KIAA0554; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(KIF3; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(LZTR-1; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Mov-34; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**NADE** (**p75NTR**-assocd. **cell death** executor); **NADE** binding proteins, and therapeutic agent **screening** method)

IT **Apoptosis**
Diagnosis
Drug **screening**
(**NADE** binding proteins, and therapeutic agent **screening** method)

IT DNA
EST (expressed sequence tag)
Guanine nucleotide exchange factors
Laminins
Transcription factors
mRNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**NIK/HGK**; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(OCRL; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(**P33 ING** relative protein; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (PTAC97; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (REP1; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Splicing factors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (SRp55-3; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (SW1/SNP complex 170 kD subunit; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (TRF1; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (TSC1; **NADE** binding proteins, and therapeutic agent **screening** method)

IT EST (expressed sequence tag)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (W75029; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (adaptins; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (autoantigens; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (cdr 2; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (cytokinesis-regulating; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (desmoplakins I; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (dynactins, 50k subunit; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Elongation factors (protein formation)

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(eEF-1; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Initiation factors (protein formation)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(eIF-4, **eIF4G**; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(endophilin; **NADE** binding proteins, and therapeutic agent **screening** method)

IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene CDC42; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Myosins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(heavy chain; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hungtingtin, **huntingtin binding** protein 1; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ligand-binding, RB binding protein II; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ligand-binding, cdc42; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ligand-binding, tax 1; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ligand-binding; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(nuclear autoantigen sperm protein; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(rab3-GAP regulatory domain; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Genetic methods
Yeast
(yeast two-hybrid method; **NADE** binding proteins, and therapeutic agent **screening** method)

IT Spectrins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.beta.-; **NADE** binding proteins, and therapeutic agent

screening method)
IT 9001-59-6, Pyruvate kinase 52660-18-1, Casein kinase 79747-53-8, Protein tyrosine phosphatase 163649-59-0, Nck-assocd. kinase 203810-05-3, Myotonic dystrophy kinase-related Cdc42-binding kinase .beta.
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**NADE** binding proteins, and therapeutic agent **screening** method)
IT 330486-92-5 330486-93-6
RL: PRP (Properties)
(unclaimed sequence; **nADE** binding proteins, and therapeutic agent **screening** method)

L24 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
2001293707 Document Number: 21264489. PubMed ID: 11278287. **14-3-3** is involved in **p75 neurotrophin receptor**-mediated signal transduction. Kimura M T; Irie S; Shoji-Hoshino S; Mukai J; Nadano D; Oshimura M; Sato T A. (Molecular Oncology Laboratory, Tsukuba Institute, RIKEN (Institute of Physical and Chemical Research), Ibaraki 305-0074, Japan.) JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 18) 276 (20) 17291-300. Journal code: HIV; 2985121R.
ISSN: 0021-9258. Pub. country: United States. Language: English.
AB The low affinity neurotrophin receptor (**p75NTR**) has been shown to mediate the **apoptosis** signaling to neural cells. However, the specific mechanisms of intracellular signal transduction of this process are largely unknown. To understand **p75NTR**-mediated signal transduction, we previously identified a protein that interacts with the intracellular domain of **p75NTR**, and we named it **p75NTR**-associated **cell death** executor (**NADE**). To elucidate further the signaling mechanisms utilized by **p75NTR** and **NADE**, we **screened** for **NADE**-binding protein(s) with the yeast two-hybrid method, and we identified 14-3-3epsilon as a **NADE**-binding protein in vivo. To examine whether 14-3-3epsilon affects the induction of **p75NTR**-mediated **apoptosis**, wild type or various deletion mutant forms of 14-3-3epsilon were co-expressed in HEK293, PC12nnr5, and oligodendrocytes.
Interestingly, transient expression of the mutant form of 14-3-3epsilon lacking the 208-255 amino acid region blocked nerve growth factor-dependent **p75NTR/NADE**-mediated **apoptosis**, although this mutant form of 14-3-3epsilon continued to associate with **NADE**. These results suggest that 14-3-3epsilon plays an important role in the modulation of nerve growth factor-dependent **p75NTR/NADE**-mediated **apoptosis**.
TI **14-3-3** is involved in **p75 neurotrophin receptor**-mediated signal transduction.
AB The low affinity neurotrophin receptor (**p75NTR**) has been shown to mediate the **apoptosis** signaling to neural cells. However, the specific mechanisms of intracellular signal transduction of this process are largely unknown. To understand **p75NTR**-mediated signal transduction, we previously identified a protein that interacts with the intracellular domain of **p75NTR**, and we named it **p75NTR**-associated **cell death** executor (**NADE**). To

elucidate further the signaling mechanisms utilized by **p75NTR** and **NADE**, we **screened** for **NADE**-binding protein(s) with the yeast two-hybrid method, and we identified 14-3-3epsilon as a **NADE**-binding protein in vivo. To examine whether 14-3-3epsilon affects the induction of **p75NTR**-mediated **apoptosis**, wild type or various deletion mutant forms of 14-3-3epsilon were co-expressed in HEK293, PC12nnr5, and oligodendrocytes. Interestingly, transient expression of the mutant form of 14-3-3epsilon lacking the 208-255 amino acid region blocked nerve growth factor-dependent **p75NTR/NADE**-mediated **apoptosis**, although this mutant form of 14-3-3epsilon continued to associate with **NADE**. These results suggest that 14-3-3epsilon plays an important role in the modulation of nerve growth factor-dependent **p75NTR/NADE**-mediated **apoptosis**.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Apoptosis: DE, drug effects
***Apoptosis: PH, physiology**
Binding Sites
Cell Line
Embryo
Gene Library
Kinetics
Mice
*Nerve Growth Factor: PD, pharmacology
*Oligodendroglia: PH, physiology
PC12 Cells
*Proteins: ME, metabolism
Rats
*Receptors, Nerve Growth Factor: PH, physiology
Recombinant Proteins: ME, metabolism
Signal Transduction: DE, drug effects
*Signal Transduction: PH, physiology
Transfection
*Tyrosine 3-Monooxygenase: ME, metabolism

CN 0 (**14-3-3** protein); 0 (Proteins); 0 (Receptors, Nerve Growth Factor); 0 (Recombinant Proteins); 0 (**p75 neurotrophin receptor**); 0 (**p75NTR**-associated **cell death** executor); EC 1.14.16.2 (Tyrosine 3-Monooxygenase)

L24 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS
1998:405979 Document No. 129:92007 Human Prt1-like subunit protein (hPrt1) and human **eIF4G**-like protein (p97) genes. Olsen, Henrik S.; Ruben, Steven M.; Sonenberg, Nahum; Imataka, Hiroaki; Methot, Nathalie; Rom, Eran (Human Genome Sciences, Inc., USA; McGill University; Olsen, Henrik S.; Ruben, Steven M.; Sonenberg, Nahum; Imataka, Hiroaki; Methot, Nathalie; Rom, Eran). PCT Int. Appl. WO 9825957 A2 19980618, 111 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,

UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US22664 19971212. PRIORITY: US 1996-33151 19961213.

AB The present invention relates to novel human Prt1 (hPrt1) and eukaryotic initiation factor 4G-like (p97) proteins which are involved in eukaryotic translation. In particular, isolated nucleic acid mols. are provided encoding the human hPrt1 and p97 proteins. The hPrt1 protein is 873 amino acids in length, shares homol. with Saccharomyces cerevisiae Prt1 protein, contains an RNA recognition motif, and interacts directly with the p170 subunit of eIF3, suggesting that it is a subunit of eIF3. The p97 protein is 907 amino acids in length, binds to eIF4A and eIF3 but not to eIF4E, and suppresses cap-dependent and cap-independent translation. HPrt1 and p97 polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same in a baculovirus expression system, and in mammalian (COS, CHO) cells. The invention further relates to **screening** methods for identifying agonists and antagonists of hPrt1 and p97 activity. Also provided are therapeutic methods for treating disease states assocd. with the hPrt1 and p97 proteins.

TI Human Prt1-like subunit protein (hPrt1) and human **eIF4G**-like protein (p97) genes

AB The present invention relates to novel human Prt1 (hPrt1) and eukaryotic initiation factor 4G-like (p97) proteins which are involved in eukaryotic translation. In particular, isolated nucleic acid mols. are provided encoding the human hPrt1 and p97 proteins. The hPrt1 protein is 873 amino acids in length, shares homol. with Saccharomyces cerevisiae Prt1 protein, contains an RNA recognition motif, and interacts directly with the p170 subunit of eIF3, suggesting that it is a subunit of eIF3. The p97 protein is 907 amino acids in length, binds to eIF4A and eIF3 but not to eIF4E, and suppresses cap-dependent and cap-independent translation. HPrt1 and p97 polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same in a baculovirus expression system, and in mammalian (COS, CHO) cells. The invention further relates to **screening** methods for identifying agonists and antagonists of hPrt1 and p97 activity. Also provided are therapeutic methods for treating disease states assocd. with the hPrt1 and p97 proteins.

ST translation factor Prt1 **eIF4G** human; sequence Prt1 **eIF4G** cDNA human

IT Initiation factors (protein formation)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(eIF-3; human Prt1-like subunit protein (hPrt1) and human **eIF4G** -like protein (p97) genes)

IT Initiation factors (protein formation)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(eIF-4G; human Prt1-like subunit protein (hPrt1) and human

eIF4G-like protein (p97) genes)
IT cDNA sequences
(for human Prt1-like subunit protein (hPrt1) and human **eIF4G**
-like protein (p97))
IT Molecular cloning
Translation initiation
(human Prt1-like subunit protein (hPrt1) and human **eIF4G**-like
protein (p97) genes)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(human Prt1-like subunit protein (hPrt1) and human **eIF4G**-like
protein (p97) genes)
IT Protein sequences
(of human Prt1-like subunit protein (hPrt1) and human **eIF4G**
-like protein (p97))
IT CHO cell
COS cell
Mammalian cells
SF9 cell
(recombinant host; human Prt1-like subunit protein (hPrt1) and human
eIF4G-like protein (p97) genes)
IT **Apoptosis**
(treatment of apoptotic diseases; human Prt1-like subunit protein
(hPrt1) and human **eIF4G**-like protein (p97) genes)
IT 187178-30-9P **209403-42-9P** 209403-47-4P 209403-48-5P
209403-50-9P **209408-43-5P**
RL: BAC (Biological activity or effector, except adverse); BPN
(Biosynthetic preparation); PRP (Properties); BIOL (Biological study);
PREP (Preparation)
(amino acid sequence; human Prt1-like subunit protein (hPrt1) and
human
eIF4G-like protein (p97) genes)
IT 186999-95-1P 209403-41-8P 209403-43-0P 209403-44-1P 209403-45-2P
209403-46-3P 209403-53-2P 209403-60-1P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PREP (Preparation)
(nucleotide sequence; human Prt1-like subunit protein (hPrt1) and
human
eIF4G-like protein (p97) genes)

L25 0 FILE MEDLINE
L26 1 FILE CAPLUS
L27 0 FILE BIOSIS
L28 0 FILE EMBASE
L29 0 FILE WPIDS
L30 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L31 1 L16 NOT L23

=> d cbib abs

L31 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

1997:138783 Document No. 126:262234 DAP-5, a novel homolog of eukaryotic translation initiation factor 4G isolated as a putative modulator of gamma interferon-induced programmed **cell death**.
Levy-Strumpf, Naomi; Deiss, Louis P.; Berissi, Hanna; Kimchi, Adi (Dep. of Molecular Genetics, Weizmann Inst. of Science, Rehovot, 76100, Israel).
Mol. Cell. Biol., 17(3), 1615-1625 (English) 1997. CODEN: MCEBD4. ISSN: 0270-7306. Publisher: American Society for Microbiology.
AB A functional approach to gene cloning was applied to HeLa cells to isolate cDNA fragments which convey resistance to gamma interferon (IFN-.gamma.)-induced programmed **cell death**. One of the rescued cDNAs, described in this work, was a fragment of a novel gene, named DAP-5. Anal. of a DAP-5 full-length cDNA clone revealed that it codes for a 97-kDa protein that is highly homologous to eukaryotic translation initiation factor 4G (**eIF4G**, also known as p220). According to its deduced amino acid sequence, this novel protein lacks the N-terminal region of **eIF4G** responsible for assocn. with the cap binding protein eIF4E. The N-terminal part of DAP-5 has 39% identity and 63% similarity to the central region of mammalian p220. Its C-terminal part is less homologous to the corresponding region of p220, suggesting that it may possess unique functional properties. The rescued DAP-5 cDNA fragment which conveyed resistance to IFN-.gamma.-induced **cell death** was expressed from the vector in the sense orientation. Intriguingly, it comprized part of the coding region which corresponds to the less conserved C-terminal part of DAP-5 and directed the synthesis of a 28-kDa miniprotein. The miniprotein exerted a dual effect on HeLa cells. Low levels of expression protected the cells from IFN-.gamma.-induced programmed **cell death**, while high levels of expression were not compatible with continuous cell growth. The relevance of DAP-5 protein to possible changes in a cell's translational machinery during programmed **cell death** and growth arrest is discussed.

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=> s sato t?/au,in;s irie s?/au,in
'IN' IS NOT A VALID FIELD CODE
L32        5300 FILE MEDLINE
L33       16988 FILE CAPLUS
L34        6433 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L35        4349 FILE EMBASE
L36        2051 FILE WPIDS
L37       25846 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L38       60967 SATO T?/AU,IN


'IN' IS NOT A VALID FIELD CODE
L39         149 FILE MEDLINE
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L40         388 FILE CAPLUS
L41         194 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L42         153 FILE EMBASE
L43          41 FILE WPIDS
L44         444 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L45        1369 IRIE S?/AU,IN

=> s l38 and l45
L46          17 FILE MEDLINE
L47          23 FILE CAPLUS
L48          24 FILE BIOSIS
L49          16 FILE EMBASE
L50           3 FILE WPIDS
L51           6 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L52          89 L38 AND L45

=> s l52 not (l16 or l23)
L53          16 FILE MEDLINE
L54          21 FILE CAPLUS
L55          24 FILE BIOSIS
L56          16 FILE EMBASE
L57           2 FILE WPIDS
L58           6 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L59          85 L52 NOT (L16 OR L23)

=> dup rem l59
PROCESSING COMPLETED FOR L59
L60          34 DUP REM L59 (51 DUPLICATES REMOVED)

=> d 1-34 cbib abs;del his y

L60  ANSWER 1 OF 34     MEDLINE
2001111743  Document Number: 20581969.    PubMed ID: 11146457.   Association
of
     smoking with apoptosis-regulated proteins (Bcl-2, bax and p53) in
resected
     non-small-cell lung cancers. Hanaoka T; Nakayama J; Mukai J; Irie
     S; Yamanda T; Sato T A. INTERNATIONAL JOURNAL OF CANCER,
     (2001 Jan 15) 91 (2) 267-9.  Journal code: GQU. ISSN: 0020-7136. Pub.
     country: United States. Language: English.

L60  ANSWER 2 OF 34  CAPLUS  COPYRIGHT 2001 ACS        DUPLICATE 1
2001:300530   Document No. 134:300837  Stable preparations for treating
     bedsore, skin ulcer and wound.  Hara, Susumu; Ebihara, Tetsuya; Koyama,
     Yohichi; Nishizawa, Masaru; Irie, Shinkichi; Sato,
     Toshiaki; Tanaka, Yoshihiro; Takigawa, Tomoaki; Yoshida, Satoshi;
     Mizuno, Keizo (Nippi, Incorporated, Japan; et al.).  PCT Int. Appl. WO
     2001028571 A1 20010426, 22 pp.  DESIGNATED STATES: W:  CN, RU, US; RW:
AT,
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BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP7335 20001020. PRIORITY: JP 1999-300330 19991022.

AB Disclosed are highly stable and safe prepns. for bedsore, skin ulcer and wound. These prepns. are obtained by blending saccharides with an iodophor and gelatin having an iodine consumption of .ltoreq. 15 mg/g measured at pH 4.5. A sheet compn. contg. povidone-iodine 3, sucrose 70, alk.-treated gelatin 1.5, KI 1, PEG 4000 5, water 1.5, and glycerin q.s. to 100 % was prepd.

L60 ANSWER 3 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

2001:74004 Document No.: PREV200100074004. Association of smoking with apoptosis-regulated proteins (Bcl-2, Bax and p53) in resected non-small-cell lung cancers. Hanaoka, Takaomi; Nakayama, Jun; Mukai, Jun; **Irie, Shinji**; Yamanda, Takeshi; **Sato, Taka-Aki (1)**. (1) Laboratory of Molecular Oncology, Department of Otolaryngology/Pathology, Columbia University, 630 West 168th St., P and S 11-451, New York, NY, 10032: TS174@columbia.edu USA. International Journal of Cancer, (15 January, 2001) Vol. 91, No. 2, pp. 267-269. print. ISSN: 0020-7136. Language: English. Summary Language: English.

L60 ANSWER 4 OF 34 MEDLINE DUPLICATE 3

2001306543 Document Number: 21157192. PubMed ID: 11257457. Overexpression of EXTL3/EXTR1 enhances NF-kappaB activity induced by TNF-alpha. Mizuno K;

Irie S; Sato T A. (Laboratory of Molecular Oncology, Tsukuba Life Science Center, The Institute of Physical and Chemical Research (RIKEN), 3-1-1 Koyadai, Ibaraki, 305-0074, Tsukuba, Japan.) CELLULAR SIGNALLING, (2001 Feb) 13 (2) 125-30. Journal code: AVB; 8904683. ISSN: 0898-6568. Pub. country: England: United Kingdom. Language:

English.

AB EXTL3/EXTR1 is a member of the EXT gene family, which may represent a class of glycosyltransferases involved in heparan sulfate biosynthesis. It is known that heparan sulfate interacts with a variety of proteins and is therefore implicated in various cellular responses. Here, we examined the effect of EXTL3 on nuclear factor-kappaB (NF-kappaB) activity stimulated by tumor necrosis factor-alpha (TNF-alpha), one of heparin-binding cytokine. The luciferase assay demonstrated that overexpression of EXTL3 enhanced TNF-alpha-induced NF-kappaB activity. This is confirmed with an electrophoretic mobility shift assay. However, EXTL3 did not affect the CD40-mediated NF-kappaB activation. The EXTL3 mutants lacking the amino terminus region failed to enhance the activity. The fluorescence of enhanced green fluorescent protein (EGFP)-fused EXTL3 was observed at the perinuclear region, whereas, the amino terminus-truncated mutant was found in a diffuse cytoplasmic region. These results suggest that EXTL3 may modulate NF-kappaB mediated by TNF-alpha.

L60 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2001 ACS

2000:152639 Document No. 132:212675 Method for inactivating endotoxins by using hydroxylated quaternary ammonium compds.. Hara, Susumu; **Sato, Takeshi**; Iwamoto, Kuniharu; **Irie, Shinkichi** (Nippi Inc.,

Japan). Jpn. Kokai Tokkyo Koho JP 2000072659 A2 20000307, 5 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1998-238897 19980825.
AB A method with endotoxin-inactivating agents, which contain hydroxylated quaternary ammonium compds. and/or their salts and bases, is claimed for prepn. of injections.

L60 ANSWER 6 OF 34 MEDLINE DUPLICATE 4
2000298829 Document Number: 20298829. PubMed ID: 10764727. NADE, a p75NTR-associated cell death executor, is involved in signal transduction mediated by the common neurotrophin receptor p75NTR. Mukai J; Hachiya T; Shoji-Hoshino S; Kimura M T; Nadano D; Suvanto P; Hanaoka T; Li Y; **Irie S**; Greene L A; **Sato T A.** (Molecular Oncology Laboratory, Tsukuba Life Science Center, RIKEN (Institute of Physical and Chemical Research), Ibaraki 305-0074, Japan.) JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Jun 9) 275 (23) 17566-70. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.
AB The low affinity neurotrophin receptor p75NTR can mediate cell survival as well as cell death of neural cells by NGF and other neurotrophins. To elucidate p75NTR-mediated signal transduction, we screened p75NTR-associated proteins by a yeast two-hybrid system. We identified one positive clone and named NADE (p75NTR-associated cell death executor). Mouse NADE has marked homology to the human HGR74 protein. NADE specifically binds to the cell-death domain of p75NTR. Co-expression of NADE and p75NTR induced caspase-2 and caspase-3 activities and the fragmentation of nuclear DNA in 293T cells. However, in the absence of p75NTR, NADE failed to induce apoptosis, suggesting that NADE expression is necessary but insufficient for p75NTR-mediated apoptosis. Furthermore, p75NTR/NADE-induced cell death was dependent on NGF but not BDNF, NT-3, or NT-4/5, and the recruitment of NADE to p75NTR (intracellular domain) was dose-dependent. We obtained similar results from PC12 cells, nnr5 cells, and oligodendrocytes. Taken together, NADE is the first signaling adaptor molecule identified in the involvement of p75NTR-mediated apoptosis induced by NGF, and it may play an important role in the pathogenesis of neurogenetic diseases.

L60 ANSWER 7 OF 34 MEDLINE DUPLICATE 5
2001086796 Document Number: 20558254. PubMed ID: 11106428. Identification of IkappaBalpha as a substrate of Fas-associated phosphatase-1. Nakai Y; **Irie S; Sato T A.** (Tsukuba Life Science Center, RIKEN (The Institute of Physical and Chemical Research), Ibaraki, Japan.) EUROPEAN JOURNAL OF BIOCHEMISTRY, (2000 Dec) 267 (24) 7170-5. Journal code: EMZ. ISSN: 0014-2956. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.
AB Fas (APO-1/CD95), a member of the tumor necrosis factor receptor (TNFR)/nerve growth factor receptor (NGFR) superfamily, is a cell-surface molecule that induces apoptosis upon activation. Fas-associated phosphatase-1 (FAP-1) is a 250-kDa protein tyrosine phosphatase (PTP) that is associated with the negative regulatory domain of Fas (C-terminal 15 amino acids). Human tumor cell lines become resistant to Fas-mediated apoptosis when transfected with FAP-1, indicating that FAP-1 functions as

a negative regulator in Fas-mediated death signaling. However, the mechanisms by which FAP-1 inhibits apoptosis are still unclear. In order to determine how FAP-1 affects the signaling mediated by Fas, we set out to identify substrates of FAP-1. Toward this end, we prepared synthetic proteins with either the catalytic domain of FAP-1 (C-terminal 399 amino acids) or its inactive form (Cys2408-->Ser) fused to glutathione-S-transferase (GST). Using an in vitro dephosphorylation reaction, we found that FAP-1 dephosphorylates IkappaBalpha. Furthermore, a substrate trapping mutant was found to bind tyrosine-phosphorylated IkappaBalpha. Taken together, our data confirm that IkappaBalpha is a substrate of FAP-1.

L60 ANSWER 8 OF 34 MEDLINE DUPLICATE 6
2000482888 Document Number: 20422682. PubMed ID: 10965021. Preparation and characterization of antibodies against human ribosomal proteins: heterogeneous expression of S11 and S30 in a panel of human cancer cell lines. Nadano D; Ishihara G; Aoki C; Yoshinaka T; **Irie S**; **Sato T A**. (Molecular Oncology Laboratory, RIKEN (Institute of Physical and Chemical Research), Tsukuba, Ibara-ki 305-0074, Japan.) JAPANESE JOURNAL OF CANCER RESEARCH, (2000 Aug) 91 (8) 802-10. Journal code: HBA; 8509412. ISSN: 0910-5050. Pub. country: Japan. Language: English.

AB Mutants of model eukaryotic organisms have revealed that most ribosomal proteins are essential for cell viability. However, the precise functional role of each ribosomal protein is largely unknown. Recent reports on the involvement of ribosomal proteins in various genetic diseases and studies on the extraribosomal functions of these proteins have cast some light on their localization and functions. Here we prepared rabbit polyclonal antibodies against 26 human ribosomal proteins; each of these reagents recognized a single band in immunoblots of the purified ribosome. We used these antibodies to evaluate a panel of human cancer cell lines. Although no deficiency of ribosomal proteins was observed, the abundance of S11 and S30 varied substantially among the cell lines, but the difference did not affect the biogenesis or composition of the ribosome. Therefore, the heterogeneity may be related to extraribosomal functions of S11 and S30. The antibodies described here are powerful tools for research into the molecular mechanisms of protein translation, cell-biological and medical studies on the ribosomal proteins, and ultimately a comprehensive understanding of all ribosomal proteins (rising dbl quote, left (low)ribosomics").

L60 ANSWER 9 OF 34 MEDLINE DUPLICATE 7
2001194316 Document Number: 20544184. PubMed ID: 11095075. Morphological changes in the nucleus and actin cytoskeleton in the process of Fas-induced apoptosis in Jurkat T cells. Maruyama W; **Irie S**; **Sato T A**. (Laboratory of Molecular Oncology, Tsukuba Life Science Center, The Institute of Physical and Chemical Research (RIKEN), Ibaraki, Japan.) HISTOCHEMICAL JOURNAL, (2000 Aug) 32 (8) 495-503. Journal code: G9A; 0163161. ISSN: 0018-2214. Pub. country: Netherlands. Language: English.

AB To investigate the early event of apoptosis, we monitored the morphological changes in the early stage of Fas-induced apoptosis in the human T-cell lymphoma cell line Jurkat, using confocal microscopy.

Morphological changes in the nuclei were observed from 30 min after stimulation, and preceded the changes in the cytoskeleton. This kind of change was enhanced in the presence of EGTA but decreased in the presence of dihydrocytochalasin B, without any changes in caspase-3 activation. During the changes in shape of the cells, the actin cytoskeleton collapsed and shrank in the center. Even though nuclei also changed their shapes in apoptotic cells, they were partially TUNEL-negative, suggesting that they were not yet damaged at the DNA level. Our results suggest that, in the process of apoptosis in Jurkat cells, cell nuclei and cytoskeleton are changed first, then membrane blebbing and caspase-3 activation occur, and fragmentation of chromosomal DNA is last.

L60 ANSWER 10 OF 34 MEDLINE DUPLICATE 8
2000404372 Document Number: 20378939. PubMed ID: 10918185. Negative regulation of Fas-mediated apoptosis by FAP-1 in human cancer cells. Li Y;
Kanki H; Hachiya T; Ohyama T; **Irie S**; Tang G; Mukai J; **Sato T**. (Department of Otolaryngology/Head and Neck Surgery, Columbia University, New York, New York, USA.) INTERNATIONAL JOURNAL OF CANCER, (2000 Aug 15) 87 (4) 473-9. Journal code: GQU; 0042124. ISSN: 0020-7136. Pub. country: United States. Language: English.
AB FAP-1 (Fas-associated phosphatase-1) was previously identified as a protein that associates with a negative regulatory domain (C-terminal 15 amino acids) of Fas using the yeast 2-hybrid system. Functional analysis indicated that FAP-1 expression correlates with resistance to Fas-induced apoptosis in human cancer cells. We first generated anti-FAP-1 polyclonal antibody and confirmed the interaction of FAP-1 and Fas in vivo. FAP-1 interacted with wild-type, but not mutant, Fas (tPLV) in 293T cells after transfecting FAP-1 and Fas or its mutant. To investigate the functional role of FAP-1 in Fas-mediated signal transduction, we established stable transfectants of FAP-1 in 3 human cancer cell lines. Apoptosis assays demonstrated that cancer cells over-expressing FAP-1 increased the resistance to Fas-induced apoptosis by the anti-Fas antibody CH-11 in contrast with the wild types or the vector-transfected cells. In addition, FAP-1 regulated the activity of both caspases 3 and 8. Our data indicate a functional role for FAP-1 as a negative regulator of Fas-mediated apoptosis in human cancer cells and suggest that an additional signal-transducing molecule may be required for complete suppression of Fas-mediated apoptosis.

L60 ANSWER 11 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
2000:202191 Document No.: PREV200000202191. Negative regulation of Fas signal transduction by FAP-1 in human cancer cells. Li, Yin (1); Tang, Guilin; **Irie, Shinji**; **Sato, Taka-Aki**. (1) Columbia Univ, New York, NY USA. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 90. Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000 ISSN: 0197-016X. Language: English. Summary Language: English.

L60 ANSWER 12 OF 34 MEDLINE DUPLICATE 9

1999358294 Document Number: 99358294. PubMed ID: 10429663. A dual topoisomerase inhibitor, TAS-103, induces apoptosis in human cancer cells.
Ohyama T; Li Y; Utsugi T; **Irie S**; Yamada Y; **Sato T**.
(Department of Otolaryngology/Head, Columbia University, New York, NY 10032, USA.) JAPANESE JOURNAL OF CANCER RESEARCH, (1999 Jun) 90 (6) 691-8. Journal code: HBA; 8509412. ISSN: 0910-5050. Pub. country: Japan. Language: English.
AB TAS-103 (6-[[2-(dimethylamino)ethyl]amino]-3-hydroxy-7H-indeno[2,1-c] quinolin-7-one dihydrochloride), a dual topoisomerase (topo) inhibitor, was developed as an anticancer agent by targeting topo I and topo II and has previously been shown to be effective against lung tumors. In this study, we investigated the cytotoxic activity of TAS-103 in various human cancer cell lines (including gastric, colon, squamous, lung, and breast cancer cells) and the induction of apoptosis by TAS-103. We next established stable transfectants of Bcl-2 in the gastric cancer cell line AZ521 and found that Bcl-2 blocked TAS-103-induced apoptosis. In addition, we demonstrated that the activities of ICE-like and CPP32-like proteases are involved in the signal transduction pathway of TAS-103-induced apoptosis. In summary, TAS-103 is a novel type of anticancer agent with a unique mechanism and could be useful as a lead compound for development of new drugs.

L60 ANSWER 13 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
1999:238445 Document No.: PREV199900238445. Identification of a 5-cM region of common allelic loss at the BRCA3 locus on 8p12-p22 in human breast cancer and genomic analysis of the hEXT1L/EXTR1/EXTL:3 gene in the locus. Suzuki, A.; Shao, X.; Song, X. Q.; Hanaoka, T.; **Irie, S.**; Kashiwada, M.; Samara, G.; Close, L. G.; Sakurada, A.; Ohuichi, N.; Satomi, S.; Fukushige, S.; **Sato, T.**; Horii, A.. Dep. Molecular Pathology, Tohoku Univ. Sch. Med., Sensai 980-8575 Japan. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 544. Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research. ISSN: 0197-016X. Language: English.

L60 ANSWER 14 OF 34 JICST-EPlus COPYRIGHT 2001 JST
1000270405 FAP-1, Acts as an Antagonist to Fas-mediated Apoptosis.. TANG G; **IRIE S; SATO T**. Riken. Nippon Gan Gakkai Sokai Kiji (Proceedings of the Japanese Cancer Association Annual Meeting). (1999) vol. 58th, pp. 502. Journal Code: G0217A) CODEN: 0546-0476; Pub. Country: Japan. Language: English.

L60 ANSWER 15 OF 34 MEDLINE DUPLICATE 10
1999357900 Document Number: 99357900. PubMed ID: 10427123. Identification of a 5-cM region of common allelic loss on 8p12-p21 in human breast cancer

and genomic analysis of the hEXT1L/EXTR1/EXTL3 gene in this locus. Suzuki A; Shao X; Song X Q; Hanaoka T; **Irie S**; Kashiwada M; Samara G; Close L G; Aoki T; Fujimori M; Ishikawa Y; Hatori M; Hosaka M; Sakurada A;
Sato M; Ohuchi N; Satomi S; Fukushige S; Horii A; **Sato T**. (Department of Molecular Pathology, Tohoku University School of Medicine, Sendai 980-8575, Japan.) INTERNATIONAL JOURNAL OF ONCOLOGY, (1999 Sep) 15
(3) 443-51. Journal code: CX5; 9306042. ISSN: 1019-6439. Pub. country: Greece. Language: English.

AB The short arm of chromosome 8 is frequently lost in many human carcinomas including breast cancer, suggesting the presence of a tumor suppressor gene(s) in this region. We identified a gene termed hEXT1L/EXTR1/EXTL3 (hEXT1L hereinafter) that was mapped to chromosome bands 8p12-p21 where frequent LOHs of this region was reported in breast cancer. The existence of the third breast cancer susceptibility gene was also suggested in this region by linkage analysis. We further performed LOH analysis in 8p12-p21 in 34 breast cancers and identified a 5-cM region of common allelic loss that overlapped with the locus for positive lod score in familial breast cancer. We further analyzed genomic alterations of hEXT1L in tumors in which frequent LOHs of 8p were reported. A total of 327 cancers (313 primary tumors and 14 cancer cell lines) including 22 primary breast cancers were analyzed, but none of the tumors had somatic mutations: only one thyroid cancer patient without any family history of cancer had a 9-bp
insertion in the constitutional DNA. These results suggest that mutations of hEXT1L do not play a major role in the development of sporadic cancers including breast cancer, and that other tumor suppressor gene(s) exists in
the 5-cM region identified in this study.

L60 ANSWER 16 OF 34 JICST-EPlus COPYRIGHT 2001 JST
1010031758 Structure functional analysis of FAP-1 in HepG2.. TANG G; MARUYAMA W; **IRIE S**; **SATO T**. Riken. Nippon Bunshi Seibutsu Gakkai Nenkai Puroguramu, Koen Yoshishu. (1999) vol. 22nd, pp. 437. Journal Code: L1278A) Pub. Country: Japan. Language: English.

L60 ANSWER 17 OF 34 MEDLINE DUPLICATE 11
2000012928 Document Number: 20012928. PubMed ID: 10544233. Functional interaction of Fas-associated phosphatase-1 (FAP-1) with p75(NTR) and their effect on NF-kappaB activation. **Irie S**; Hachiya T; Rabizadeh S; Maruyama W; Mukai J; Li Y; Reed J C; Bredesen D E; **Sato T A**. (Molecular Oncology Laboratory, Tsukuba Life Science Center, Institute of Physical and Chemical Research (RIKEN), Ibaraki, Japan.. irie@rtc.riken.go.jp) . FEBS LETTERS, (1999 Oct 29) 460 (2) 191-8. Journal code: EUH; 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB The common neurotrophin receptor p75(NTR), a member of the tumor necrosis factor (TNF) receptor superfamily, plays an important role in several cellular signaling cascades, including that leading to apoptosis. FAP-1 (Fas-associated phosphatase-1), which binds to the cytoplasmic tail of Fas, was originally identified as a negative regulator of Fas-mediated apoptosis. Here we have shown by co-immunoprecipitation that FAP-1 also binds to the p75(NTR) cytoplasmic domain in vivo through the interaction between the third PDZ domain of FAP-1 and C-terminal Ser-Pro-Val residues

of p75(NTR). Furthermore, cells expressing a FAP-1/green fluorescent protein showed intracellular co-localization of FAP-1 and p75(NTR) at the plasma membrane. To elucidate the functional role of this physical interaction, we examined TRAF6 (TNF receptor-associated factor 6)-mediated NF-kappaB activation and tamoxifen-induced apoptosis in 293T cells expressing p75(NTR). The results revealed that TRAF6-mediated NF-kappaB activation was suppressed by p75(NTR) and that the p75(NTR)-mediated NF-kappaB suppression was reduced by FAP-1 expression. Interestingly, a mutant of the p75(NTR) intracellular domain with a single substitution of a Met for Val in its C-terminus, which cannot interact with FAP-1, displayed enhanced pro-apoptotic activity in 293T transfected cells. Thus, similar to Fas, FAP-1 may be involved in suppressing p75(NTR)-mediated pro-apoptotic signaling through its interaction with three C-terminal amino acids (tSPV). Thus, FAP-1 may regulate p75(NTR)-mediated signal transduction by physiological interaction through its third PDZ domain.

L60 ANSWER 18 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
1999:173365 Document No.: PREV199900173365. Attenuation of Fas-mediated apoptosis by FAP-1: FAP-1 is involved in Fas-mediated apoptosis as a negative regulator in human T cell leukemia and gastric cancer cell lines.
Li, Yin (1); Kanki, Hiroaki (1); Ohyama, Tomoko (1); **Irie, Shinji ; Sato, Taka-Aki (1)**. (1) Columbia Univ., New York, NY 10032 USA. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 172. Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research. ISSN: 0197-016X. Language: English.

L60 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 12
1999:207097 Document No. 130:350431 Defense mechanism of cancer in apoptosis. Shimada-Matsumoto, Hiroko; **Irie, Shinji; Sato, Takaaki** (Tsukuba Life Sci. Cent., Inst. Phys. Chem. Res., Tsukuba, 305-0074, Japan). Baiosaiensu to Indasutori, 57(3), 161-166 (Japanese) 1999. CODEN: BIDSE6. ISSN: 0914-8981. Publisher: Baioindasutori Kyokai.
AB A review with 34 refs. Physiol. significance and morphol. changes upon apoptosis are depicted, and apoptosis relates with several diseases such as virus infection, Alzheimer's disease and autoimmune diseases. Signal transduction from tumor necrosis factor (TNF)/nerve growth factor (NGF) receptor family, which triggers apoptosis. Bcl-2 and p53 participate in suppression of apoptosis in tumor. Fas-assocd. phosphatase-1 (FAP-1) binds neg.- regulatory region of Fas, and is expressed in apoptosis-resistant tissues such as kidney, lung, ovary and testis. Several anti-tumor drugs are known to induce apoptosis.

L60 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 13
1998:79630 Document No. 128:135312 Metal conductor interconnection in semiconductor device. **Irie, Seishi**; Sato, Takahiro (Toshiba Micro Electronics K. K., Japan; Toshiba Corp.). Jpn. Kokai Tokkyo Koho JP 10032200 A2 19980203 Heisei, 5 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1996-185794 19960716.

AB The invention relates to a semiconductor device having metal conductor patterns and passivation film, wherein the presence of cavities in the passivation films does not lead to foaming in the photoresists.

L60 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 14
1998:425463 Document No. 129:174741 Characteristics and market trends of collagen as a food material. **Sato, Takeshi**; Koyama, Yoh-ichi; Suzuki, Koki; **Irie, Shinkichi** (Nippi Res. Inst. Biomatrix, Nippi Inc., Tokyo, 120-860, Japan). Hikaku Kagaku (Sci.), 44(1), 11-18 (Japanese) 1998. CODEN: HIKAEJ. ISSN: 0018-1811. Publisher: Nippon Hikaku Gijutsu Kyokai.
AB A review with 28 refs. Collagen is the most abundant protein in animal tissues and its denatured form is well known as gelatin. The digested gelatin peptides are widely used as an ingredient of health food, while the use of collagen is mostly restricted to sausage casing. In order to augment the usefulness of collagen, it is necessary (1) to develop novel collagen materials from various sources, (2) to create complex materials made of collagen and other natural mols. of high mol. wt., and (3) to reveal new physiol. functions of collagen.

L60 ANSWER 22 OF 34 MEDLINE DUPLICATE 15
97001150 Document Number: 97001150. PubMed ID: 8812483. Cloning of cDNAs encoding the human BAG1 protein and localization of the human BAG1 gene to
chromosome 9p12. Takayama S; Kochel K; **Irie S**; Inazawa J; Abe T; **Sato T**; Druck T; Huebner K; Reed J C. (Bumham Institute, La Jolla, California 92037, USA.) GENOMICS, (1996 Aug 1) 35 (3) 494-8. Journal code: GEN; 8800135. ISSN: 0888-7543. Pub. country: United States. Language: English.
AB cDNAs encoding the human homolog of BAG1, a Bcl-2-binding protein with anti-apoptotic function, were cloned. DNA sequence analysis of human BAG1 cDNAs predicts a protein with an additional 55 amino acids at its NH2-terminus compared to the mouse protein. Immunoblot assays using monoclonal antibodies raised against bacterially produced h-BAG1 protein confirmed the larger size of the human protein (approximately 34 kDa) compared to mouse. PCR analysis of DNA from human x rodent somatic cell hybrids using human BAG1-specific primers localized the gene to human chromosome 9. Cosmid clones of h-BAG1 were obtained and used for fluorescence in situ hybridization analysis of normal metaphase chromosomes, thus localizing h-BAG1 to 9p12, a region associated with hereditary disorders that may involve developmental dysregulation of programmed cell death.

L60 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2001 ACS
1995:411833 Document No. 123:104250 Interactions among members of the Bcl-2 protein family analyzed with a yeast two-hybrid system. [Erratum to document cited in CA121:294306]. **Sato, Takaaki**; Hanada, Motoi; Bodrug, Sharon; **Irie, Shinji**; Iwama, Natsuko; Boise, Lawrence H.; Thompson, Craig B.; Golemis, Erica; Fong, Linda; et al. (Oncogene Tumor Supressor Gene Program, La Jolla Cancer Research Foundation, La Jolla, CA, 92037, USA). Proc. Natl. Acad. Sci. U. S. A., 92(5), 1794 (English) 1995. CODEN: PNASA6. ISSN: 0027-8424.
AB The errors were not reflected in the abstr. or the index entries.

L60 ANSWER 24 OF 34 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

95079412 EMBASE Document No.: 1995079412. Erratum: Interactions among members
of the Bcl-2 protein family analyzed with a yeast two-hybrid system (Proceedings of the National Academy of Sciences of the United States of America (September 27, 1994) 91 (9238- 9242)). **Sato T.**; Hanada M.; Bodrug S.; **Irie S.**; Iwama N.; Boise L.H.; Thompson C.B.; Golemis E.; Fong L.; Wang H.-G.; Reed J.C.. Proceedings of the National Academy of Sciences of the United States of America 92/5 (1794) 1995. ISSN: 0027-8424. CODEN: PNASA6. Pub. Country: United States. Language: English.

L60 ANSWER 25 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
1995:385203 Document No.: PREV199598399503. FAP-1, a protein tyrosine phosphatase that associates with Fas. **Sato, T.; Irie, S.** ; Kitada, S.; Reed, J. C.. La Jolla Cancer Res. Foundation, La Jolla, CA 92037 USA. 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 776. The 9th International Congress of Immunology. Publisher: 9th International Congress of Immunology San Francisco, California, USA. Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies San Francisco, California, USA July 23-29, 1995 Language: English.

L60 ANSWER 26 OF 34 MEDLINE DUPLICATE 16
95232528 Document Number: 95232528. PubMed ID: 7536343. FAP-1: a protein tyrosine phosphatase that associates with Fas. **Sato T; Irie S**; Kitada S; Reed J C. (La Jolla Cancer Research Foundation, Oncogene and Tumor Suppressor Gene Program, CA 92037, USA.) SCIENCE, (1995 Apr 21)
268 (5209) 411-5. Journal code: UJ7; 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.
AB Fas is a cell surface receptor that controls a poorly understood signal transduction pathway that leads to cell death by means of apoptosis. A protein tyrosine phosphatase, FAP-1, capable of interacting with the cytosolic domain of Fas, was identified. The carboxyl terminal 15 amino acids of Fas are necessary and sufficient for interaction with FAP-1. FAP-1 expression is highest in tissues and cell lines that are relatively resistant to Fas-mediated cytotoxicity. Gene transfer-mediated elevations in FAP-1 partially abolished Fas-induced apoptosis in a T cell line. These findings are consistent with an inhibitory effect of FAP-1 on Fas signal transduction.

L60 ANSWER 27 OF 34 MEDLINE DUPLICATE 17
95136360 Document Number: 95136360. PubMed ID: 7834747. Cloning and functional analysis of BAG-1: a novel Bcl-2-binding protein with anti-cell
death activity. Takayama S; **Sato T**; Krajewski S; Kochel K; **Irie S**; Millan J A; Reed J C. (La Jolla Cancer Research Foundation, California 92037.) CELL, (1995 Jan 27) 80 (2) 279-84. Journal code: CQ4; 0413066. ISSN: 0092-8674. Pub. country: United States. Language: English.
AB Using a protein interaction cloning technique, we identified cDNAs that encode a novel Bcl-2-binding protein, termed BAG-1. The BAG-1 protein shares no significant homology with Bcl-2 or other Bcl-2 family proteins, which can form homo- and heterodimers. In gene transfer experiments using

a human lymphoid cell line, Jurkat, coexpression of BAG-1 and Bcl-2 provided markedly increased protection from cell death induced by several stimuli, including staurosporine, anti-Fas antibody, and cytolytic T cells, relative to cells that contained gene transfer-mediated elevations in either BAG-1 or Bcl-2 protein alone. BAG-transfected 3T3 fibroblasts also exhibited prolonged cell survival in response to an apoptotic stimulus. The findings indicate that bag-1 represents a new type of anti-cell death gene and suggest that some routes of apoptosis induction previously ascribed to Bcl-2-independent pathways may instead reflect a need for the combination of Bcl-2 and BAG-1.

L60 ANSWER 28 OF 34 MEDLINE DUPLICATE 18
95129692 Document Number: 95129692. PubMed ID: 7530216. A novel member of
the TRAF family of putative signal transducing proteins binds to the cytosolic domain of CD40. **Sato T; Irie S;** Reed J C.
(La Jolla Cancer Research Foundation, Oncogene & Tumor Suppressor Gene Program, CA 92037.) FEBS LETTERS, (1995 Jan 23) 358 (2) 113-8. Journal code: EUH; 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.
AB CD40 is a member of the tumor necrosis factor receptor (TNF-R) family that
regulates B-lymphocyte proliferation, immunoglobulin class-switching, and apoptosis through poorly defined signal transduction mechanisms. Using a yeast two-hybrid method, cDNAs were obtained that encode a novel protein, CD40-associated protein-1 (CAP-1), which binds specifically to the cytosolic domain of CD40 but not TNF-R1, TNF-R2, or Fas. The CAP-1 protein
contains a C-terminal domain that shares strong amino acid sequence homology with a unique domain found recently in two putative signal transducing proteins that bind to the TNF-R2 cytosolic tail, TRAF1 and TRAF2. This C-terminal region of CAP-1 was sufficient to mediate binding to CD40 and homodimerization of CAP-1 proteins. The N-terminal portion of CAP-1 contains a RING finger motif and three zinc finger-like domains similar to those found in several regulatory proteins that interact with DNA or RNA. CAP-1 thus represents a new member of a family of potential signal transducing proteins that contain a conserved domain (the TRAF domain), bind to the cytosolic regions of particular members of TNF-R family proteins, and that can form homo- and heterotypic dimers.

L60 ANSWER 29 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
1995:190077 Document No.: PREV199598204377. Investigations of interactions between members of the Bcl-2 protein family using yeast two-hybrid system.
Sato, Takaaki; Kobayashi, Hiroko; Hanada, Motoi; Bodrug, Sharon; **Irie, Shinji;** Wang, Hong-Gang; Reed, John C.. La Jolla Cancer Res. Found., Oncogene Tumor Suppressor Gene Program, La Jolla, CA 92037 USA. Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 19A, pp. 76. Meeting Info.: Keystone Symposium on Oncogenes: 20 Years Later Keystone, Colorado, USA January 5-11, 1995 ISSN: 0733-1959. Language: English.

L60 ANSWER 30 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
1995:189920 Document No.: PREV199598204220. A novel cDNA encoding a protein that binds the cytoplasmic domain of CD40. **Irie, Shinji;**

Sato, Takaaki; Reed, John C.. La Jolla Cancer Res. Found., La Jolla, CA 92037 USA. Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 19A, pp. 36. Meeting Info.: Keystone Symposium on Oncogenes: 20 Years Later Keystone, Colorado, USA January 5-11, 1995 ISSN: 0733-1959.
Language: English.

L60 ANSWER 31 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
1995:150749 Document No.: PREV199598165049. Molecular cloning and characterization of a novel Bcl-2-binding protein, Bag-1. Takayama, S.; **Sato, T.**; Kochel, K.; Krajewski, S.; **Irie, S.**; Reed, J. C.. La Jolla Cancer Res. Found., La Jolla, CA 92037 USA. Proceedings of the American Association for Cancer Research Annual Meeting, (1995) Vol. 36, No. 0, pp. 9. Meeting Info.: Eighty-sixth Annual Meeting of the American Association for Cancer Research Toronto, Ontario, Canada March 18-22, 1995 ISSN: 0197-016X. Language: English.

L60 ANSWER 32 OF 34 MEDLINE DUPLICATE 19
95023886 Document Number: 95023886. PubMed ID: 7937747. Interactions among members of the Bcl-2 protein family analyzed with a yeast two-hybrid system. **Sato T**; Hanada M; Bodrug S; **Irie S**; Iwama N; Boise L H; Thompson C B; Golemis E; Fong L; Wang H G; +. (La Jolla Cancer Research Foundation, CA 92037.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Sep 27) 91 (20) 9238-42. Journal code: PV3; 7505876. ISSN: 0027-8424. Pub. country: United States.
Language: English.
AB Interactions of the Bcl-2 protein with itself and other members of the Bcl-2 family, including Bcl-X-L, Bcl-X-S, Mcl-1, and Bax, were explored with a yeast two-hybrid system. Fusion proteins were created by linking Bcl-2 family proteins to a LexA DNA-binding domain or a B42 trans-activation domain. Protein-protein interactions were examined by expression of these fusion proteins in Saccharomyces cerevisiae having a lacZ (beta-galactosidase) gene under control of a LexA-dependent operator.
This approach gave evidence for Bcl-2 protein homodimerization. Bcl-2 also interacted with Bcl-X-L and Mcl-1 and with the dominant inhibitors Bax and Bcl-X-S. Bcl-X-L displayed the same pattern of combinatorial interactions with Bcl-2 family proteins as Bcl-2. Use of deletion mutants of Bcl-2 suggested that Bcl-2 homodimerization involves interactions between two distinct regions within the Bcl-2 protein, since a LexA protein containing Bcl-2 amino acids 83-218 mediated functional interactions with a B42 fusion protein containing Bcl-2 amino acids 1-81 but did not complement a B42 fusion protein containing Bcl-2 amino acids 83-218. In contrast to LexA/Bcl-2 fusion proteins, expression of a LexA/Bax protein was lethal to yeast. This cytotoxicity could be abrogated by B42 fusion proteins containing Bcl-2, Bcl-X-L, or Mcl-1 but not those containing Bcl-X-S (an alternatively spliced form of Bcl-X that lacks a well-conserved 63-amino acid region). The findings suggest a model whereby Bax and Bcl-X-S differentially regulate Bcl-2 function, and indicate that requirements for

Bcl-2/Bax heterodimerization may be different from those for Bcl-2/Bcl-2 homodimerization.

L60 ANSWER 33 OF 34 MEDLINE DUPLICATE 20
94193015 Document Number: 94193015. PubMed ID: 8144041. Cloning and sequencing of a cDNA encoding the rat Bcl-2 protein. **Sato T;** **Irie S;** Krajewski S; Reed J C. (La Jolla Cancer Research Foundation, Cancer Research Center, CA 92037.) GENE, (1994 Mar 25) 140 (2) 291-2. Journal code: FOP; 7706761. ISSN: 0378-1119. Pub. country: Netherlands. Language: English.

AB A rat cDNA encoding the Bcl-2 protein was cloned and sequenced. The primary amino-acid sequence deduced from the nucleotide sequence reveals a 236-aa protein having extensive homology with the mouse (95%), human (87%) and chicken (71%) Bcl-2 proteins.

L60 ANSWER 34 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
1994:287829 Document No.: PREV199497300829. Molecular cloning and characterization of a novel BCL-2-binding protein, BAP-1. Takayama, S.; **Sato, T.**; Krajewski, S.; **Irie, S.**; Reed, J. C.. La Jolla Cancer Res. Found., La Jolla, CA 92037 USA. Proceedings of the American Association for Cancer Research Annual Meeting, (1994) Vol. 35, No. 0, pp. 8. Meeting Info.: 85th Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 10-13, 1994 ISSN: 0197-016X. Language: English.